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09/891,750	06/26/2001	Kevin Joseph Moriarty	QA0239ACIP	2728

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EXAMINER
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ART UNIT	PAPER NUMBER
1624	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/891,750	Applicant(s) MORIARTY ET AL.	
	Examiner Venkataraman Balasubramanian	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *8-11,13 and 18-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,12,14-17 and 27-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election of Group I, claims 1-7,12, 14-17 and 31-51 in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8-11,13 and 18-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group V.

Claims 1-7,12, 14-17 and 31-51 will be examined to the extent they embrace the elected subject matter. Since applicants have elected method of use claim 27, the dependent claims 28-30 will be rejoined with Group I and will be examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7,12,14-17 and 27-51 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim.

1. Recitation of the term "including" in claims 1-7, 12, 14-17 and 27-51, renders these claims indefinite. The transitional term "including" which is synonymous with "containing," or "comprising", "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. "Containing" is a term of art used in claim language which means that the named

elements are essential, but other elements may be added and still form a construct within the scope of the claim "comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts". See MPEP 2111.03. Similarly recitation of the term 'containing" in claims 3-4 and 8, renders these claims indefinite for the same reason stated above.

2. In claims 1-7, 12, 14-17 and 27-51, recitation of the term "prodrugs' is deemed as indefinite for more than one reason. First of all, the term is recited in plural and there is singular plural mismatch in these claims. Note if recited in plural the claim will be limited to composition as it has more than one ingredient.

Moreover, prodrugs in general and as noted in specification, are compounds, which undergo in vivo hydrolysis to parent active drugs. In that sense recitation of prodrugs is acceptable. However, the definition of various R groups include such groups, namely esters, alkoxycabonyl etc. and therefore it is not clear what is the difference between these variable groups and the prodrug groups.

3. In claims 1-7, 12, 14-17 and 27-51, the recitation of "isomers, enatiomers, diastereomers, tautomers, pharmaceutically acceptable salts, prodrugs and solvates" in plural renders these claims indefinite as to nature of these claims. Are they meant to be composition claims?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for rheumatoid arthritis, does not reasonably provide enablement for any or all p38 mediated diseases/ disorders including those yet to be discovered as due to p38. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.

The instant claims 19-30 are drawn to "treating a condition associated with p38 activity ". The scope of the claims includes not only any or all conditions but also those condition yet to be discovered as mediated by p38 for which there is no enabling disclosure. In addition, the scope of these claims includes treatment of various diseases, which is not adequately enabled solely based on the inhibiting p38 activity of the compounds provided in the specification at pages 19-20. The instant compounds are disclosed to have inhibiting p38 activity and it is recited that the instant compounds are therefore useful in treating any or all diseases where p38 activity is implicated, for which applicants provide no competent evidence. Furthermore, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as Alzheimer's disease, multiple sclerosis, psoriasis etc. are very difficult to treat and at present there is no known drug, which can successfully reverse the course of these diseases, despite the fact that there are many drugs, which can be used for "inflammatory condition". Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided.

See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating diseases that require inhibiting p38 activity. See Henry et al. cited in the Information Disclosure Statement.

2) The state of the prior art: A very recent publication expressed that treating disease by the inhibition of p38 is still exploratory.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical

use for r treating any or all condition of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all condition and the state of the art is that the effects of inhibiting p38 activity are unpredictable and at best limited to modulation of rheumatoid arthritis.

6) The breadth of the claims: The instant claims embrace any or all condition including those yet to be related to p38 activity.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of receptor-ligand interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,14 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Schmitz et al. US 3,290,305.

Schmitz et al. teaches several trisubstituted triazines, which include compounds, claimed generically in the instant claims, for use as disinfectants.

See formula I on col. 2 and note the definition of X, Y and Z. See the first compound on col. 3.

Claims 1, 2, 14 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Winter et al. US 3,867,383.

Winter et al. teaches several trisubstituted triazines, which include compounds, claimed generically in the instant claims, for use as cardiovascular agents.

See formula I on col.1 and note the definition of Z and R". See examples 2, 3, 4,5 and 6 for compounds made.

Claims 1, 2, 14 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoppe et al. US 3,867,383.

Hoppe et al. teaches several trisubstituted triazines, which include compounds, claimed generically in the instant claims, for use as sunscreen agents.

See formula I on claim 1 and note the definition of R. See examples 1-8 for compounds made.

Claims 1, 2, 14 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Newton et al. US 5,062,882.

Newton et al. teaches several trisubstituted triazines, which include compounds, claimed generically in the instant claims, for use as herbicides.

See formula I on col. 1 and note the definition of Z, Y, R^1 and R^2 . See examples 1-67 and Table I for compounds made.

Claims 1, 2, 14 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Raspanti et al. US 5,346,791.

Raspanti et al. teaches several trisubstituted triazines, which include compounds, claimed generically in the instant claims, for use as light stabilizers

See formula I on col. 1 and note the definition of X, R, R_1 and R_2 . See examples 1-40 and Table I for compounds made.

Claims 1, 2, 14 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Raspanti et al. US 5,759,525.

Raspanti et al. teaches use trisubstituted triazine, which includes compound, claimed generically in the instant claims, for use as light stabilizers

See compound of formula I on col. 1.

Claims 1, 2, 14 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Raspanti et al. US 5,801,244.

Raspanti et al. teaches several trisubstituted triazines, which include compounds, claimed generically in the instant claims, for use as light stabilizers

See formula I on col. 1 and note the definition of various R groups. See examples 1-5 for compounds made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 14 and 31-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daeyaert et al US 6,150,360.

Daeyaert et al. teaches several trisubstituted triazines, which include compounds, claimed herein for use as anti-HIV agents. See col. 1, formula I and note the definition of L, R^1, R^2, R^3, R^4 and n. See col. 3-10 for various preferred

embodiments and col. 10-14 for processes of making them. See col. 17-27 for examples and Table 2 for compounds made.

Claims rejected herein require a carboxy or carboxamide or nitro group in the aryl ring in addition to other substituents in the triazine ring while Daeyaert et al. teaches a cyano group.

However Daeyaert et al et al. teaches the equivalency of exemplified cyano group in the benzene ring and other substituents in the triazine ring shown in examples 1-82 shown in Table 2 with those contemplated and claimed in the definition of various variable groups and R^4 groups of formula I. See col. 1, formula I and note the definition of L, R^1, R^2, R^3, R^4 and n. Note R^4 includes carboxy or carboxamide or nitro groups. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds with triazine core variously substituted in said ring as permitted by the reference and expect resulting compounds (instant compounds) to possess the uses taught by the art in view of the equivalency teaching outline above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 12, 14-17 and 28-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 12 and 14-41 of copending Application No. 09/747,195. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter embraced in the instant claims is also embraced in the copending application..

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

References cited in Information Disclosure Statement (paper # 4) are made of record.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V. Balasubramanian
Venkataraman Balasubramanian

6/15/2002